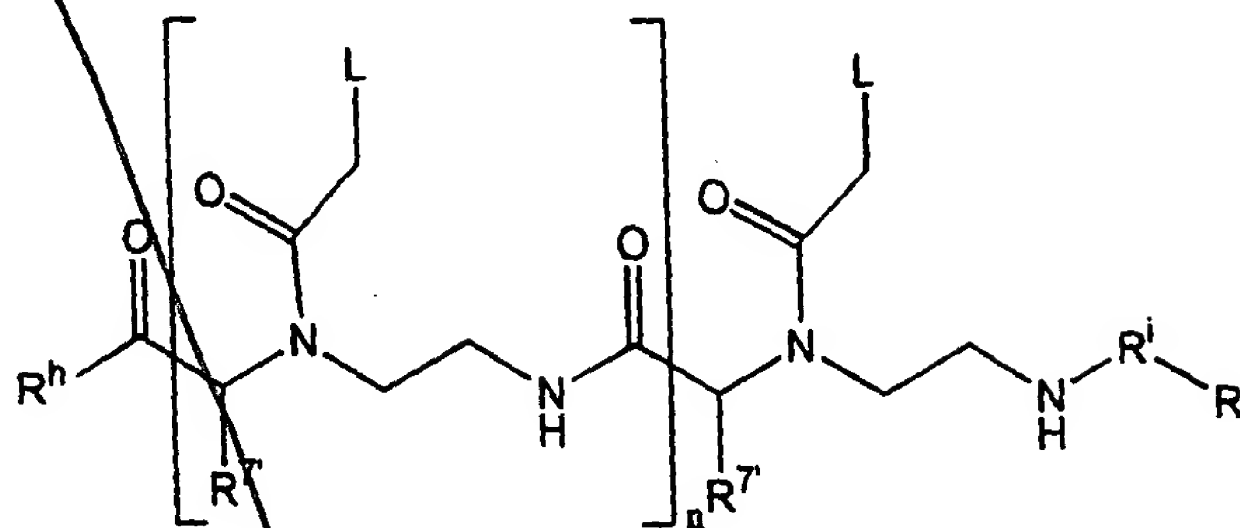


## What is claimed is:

1. A peptide nucleic acid having formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each  $R^7$  is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid, at least one  $R^7$  being the side chain of a naturally-occurring or non-naturally-occurring amino acid;

$R^h$  is OH,  $NH_2$ , or  $NH-Lys-NH_2$ ;

each of  $R^i$  and  $R^j$  is, independently, a lipophilic group or an amino acid labeled with a fluorescent group; or  $R^i$  and  $R^j$ , together, are a lipophilic group; and

n is an integer from 1 to 30.

2. The peptide nucleic acid of claim 1 wherein at least one of said  $R^7$  is the side chain of a naturally-occurring amino acid.

3. The peptide nucleic acid of claim 2 wherein at least one  $R^7$  is the side chain of D-lysine.

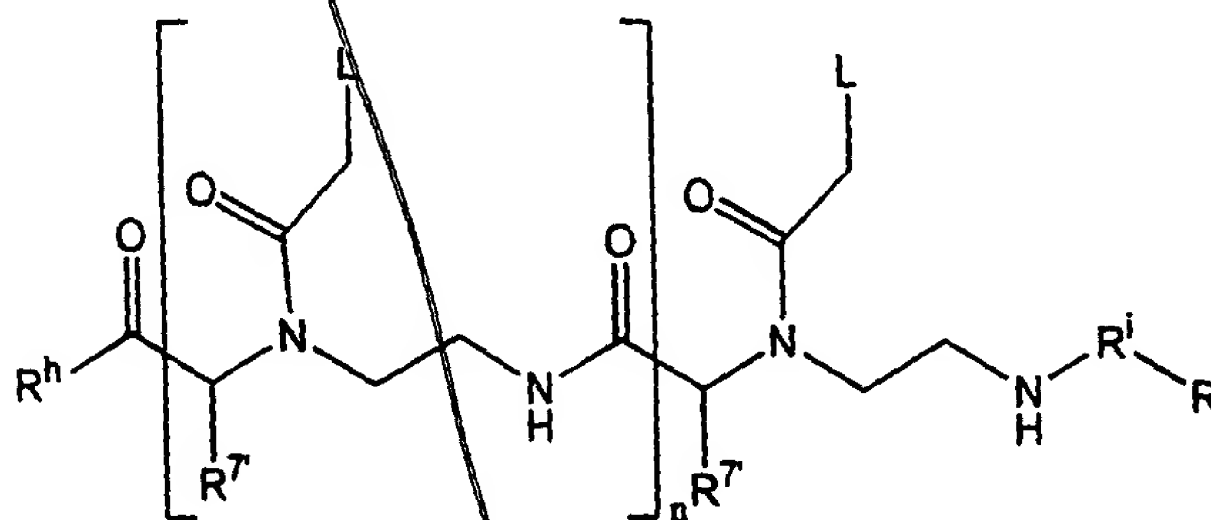
4. The peptide nucleic acid of claim 1 wherein  $R^i$  is D-lysine labeled with a fluorescent group and  $R^j$  is an adamantoyl group.

5. The peptide nucleic acid of claim 4 wherein said fluorescent group is fluorescein.

6. The peptide nucleic acid of claim 1 wherein  $R^i$  and  $R^j$ , together, are an adamantoyl group.

7. The peptide nucleic acid of claim 1 wherein  $R^7$  is the side chain of an amino acid and the carbon atom to which the side chain is attached is stereochemically enriched.

8. A composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:



wherein:

each  $L$  is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each  $R^7$  is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid;

$R^h$  is  $OH$ ,  $NH_2$ , or  $NH(Lys)NH_2$ ;

each of  $R^i$  and  $R^j$  is, independently, a lipophilic group or an amino acid labeled with a fluorescent group; or  $R^i$  and  $R^j$ , together, are a lipophilic group; and

$n$  is an integer from 1 to 30.

9. The composition of claim 8 wherein at least one of said  $R^7$  is the side chain of a naturally-occurring amino acid.

10. The composition of claim 9 wherein said amino acid is D-lysine.

11. The composition of claim 8 wherein  $R^i$  is D-lysine labeled with a fluorescent group and  $R^j$  is an adamantoyl group.

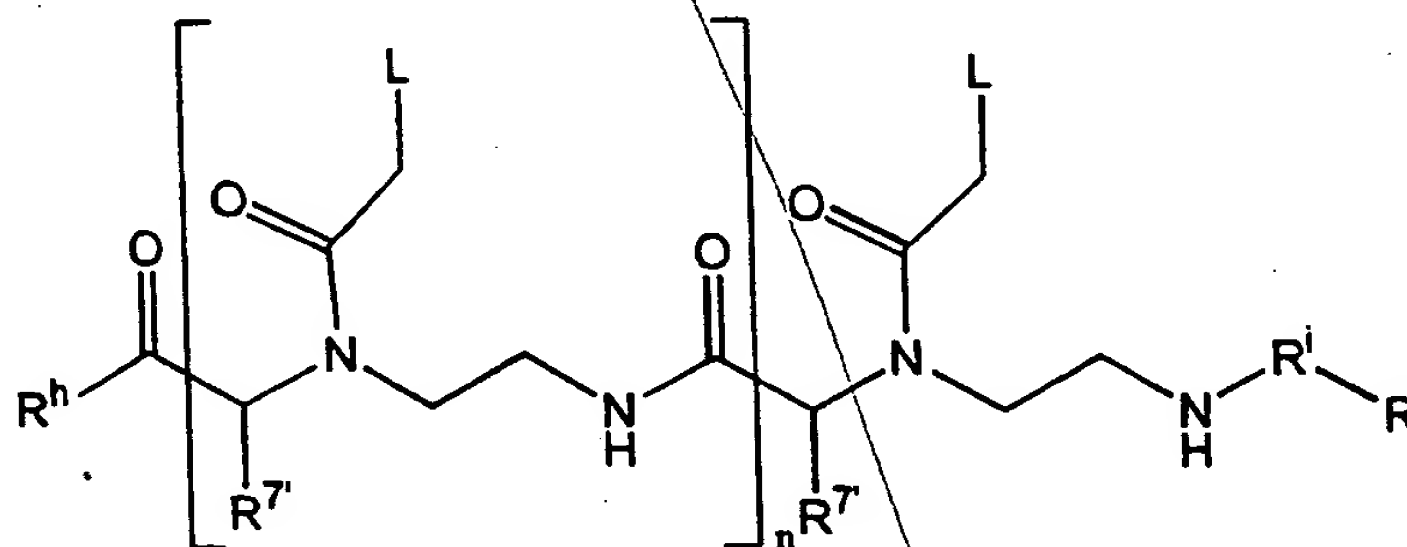
12. The composition of claim 11 wherein said fluorescent group is fluorescein.
13. The composition of claim 8 wherein  $R^1$  and  $R^1$ , together, are an adamantoyl group.
14. The composition of claim 8 wherein  $R^7$  is the side chain of an amino acid and the carbon atom to which the side chain is attached is stereochemically enriched.
- SUB D<sub>2</sub> 15. A method of modulating cellular uptake and distribution of a peptide nucleic acid comprising the steps of:
- (a) derivatizing a backbone position of said peptide nucleic acid; and
  - (b) conjugating the derivatized peptide nucleic acid of step (a) with a lipophilic group.
16. The method of claim 15 wherein said derivatizing comprises attaching the side chain of at least one naturally-occurring or non-naturally-occurring amino acid to the backbone of said peptide nucleic acid.
17. The method of claim 16 wherein said derivatizing comprises attaching the side chain of a naturally-occurring amino acid to the backbone of said peptide nucleic acid.
18. The method of claim 17 wherein said amino acid is D-lysine.
19. The method of claim 15 wherein said lipophilic group is an adamantyl group.
20. The method of claim 15 further comprising introducing the peptide nucleic acid of step (b) into liposomes.
- SUB D<sub>2</sub> 21. A method of modulating cellular uptake and distribution of a peptide nucleic acid comprising the steps of:
- (a) conjugating said peptide nucleic acid with a lipophilic group; and
  - (b) introducing the conjugated peptide nucleic acid of step (a) into liposomes.

22. The method of claim 21 wherein said lipophilic group is an adamantyl group.

23. A pharmaceutical composition comprising the peptide nucleic acid according to claim 1 and at least one pharmaceutically acceptable carrier, binder, thickener, diluent, buffer, preservative or surface active agent.

24. A pharmaceutical composition comprising the composition of claim 8 and at least one pharmaceutically acceptable carrier, binder, thickener, diluent, buffer, preservative or surface active agent.

25. A method of modulating cellular uptake and distribution of a peptide nucleic acid in a cell or tissue comprising administering to the cell or tissue a peptide nucleic acid having formula:



**wherein:**

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each R<sup>7</sup> is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid, at least one R<sup>7</sup> being the side chain of a naturally-occurring or non-naturally-occurring amino acid;

$R^b$  is OH,  $NH_2$ , or  $NHLysNH_2$ .

each of R<sup>i</sup> and R<sup>j</sup> is, independently, a lipophilic group or an amino acid labeled with a fluorescent group; or R<sup>i</sup> and R<sup>j</sup>, together, are a lipophilic group; and

**n is an integer from 1 to 30.**

26. The method of claim 25 wherein at least one of said  $R^7$  is the side chain of

a naturally-occurring amino acid.

27. The method of claim 26 wherein said amino acid is D-lysine.

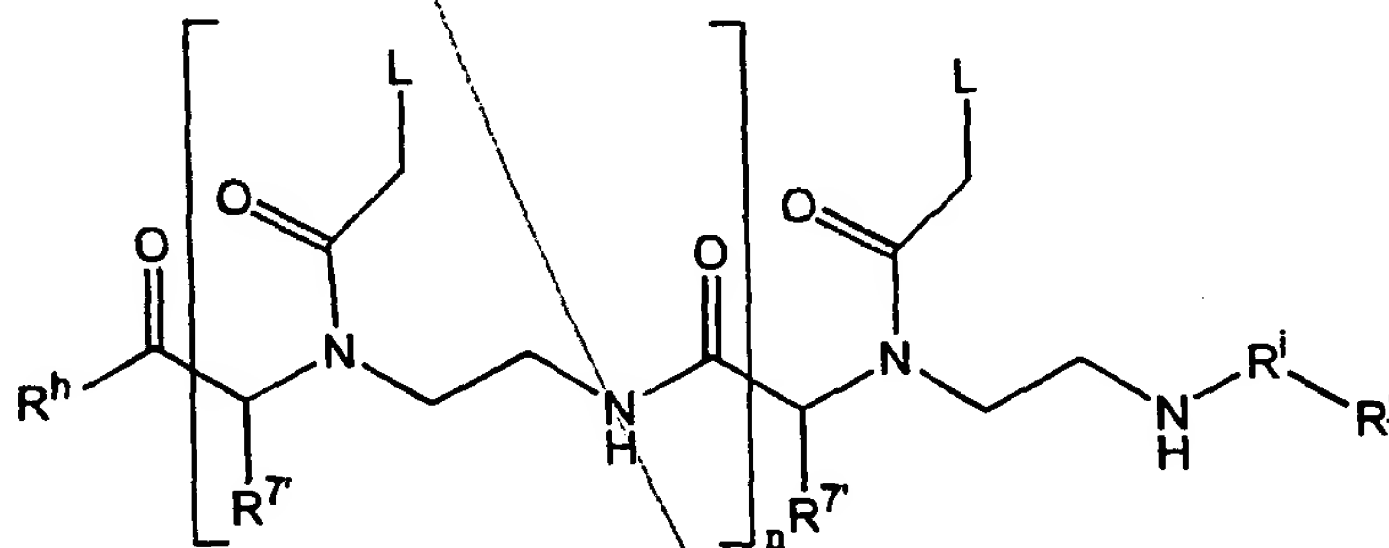
28. The method of claim of claim 25 wherein  $R^i$  is D-lysine labeled with a fluorescent group and  $R^j$  is an adamantoyl group.

29. The method of claim 28 wherein said fluorescent group is fluorescein.

30. The method of claim 25 wherein  $R^i$  and  $R^j$ , together, are an adamantoyl group.

31. The method of claim 25 wherein  $R^7$  is the side chain of an amino acid and the carbon atom to which the side chain is attached is stereochemically enriched.

32. A method of modulating cellular uptake and distribution of a peptide nucleic acid in a cell or tissue comprising administering to the cell or tissue a composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each  $R^7$  is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid;

$R^h$  is OH,  $NH_2$ , or  $NHLysNH_2$ ;

each of  $R^i$  and  $R^j$  is, independently, a lipophilic group or an amino acid labeled with

*SUB 4 control*  
 a fluorescent group; or  $R^i$  and  $R^j$ , together, are a lipophilic group; and  
 $n$  is an integer from 1 to 30.

33. The method of claim 32 wherein at least one of said  $R^7$  is the side chain of a naturally-occurring amino acid.

34. The method of claim 33 wherein said amino acid is D-lysine.

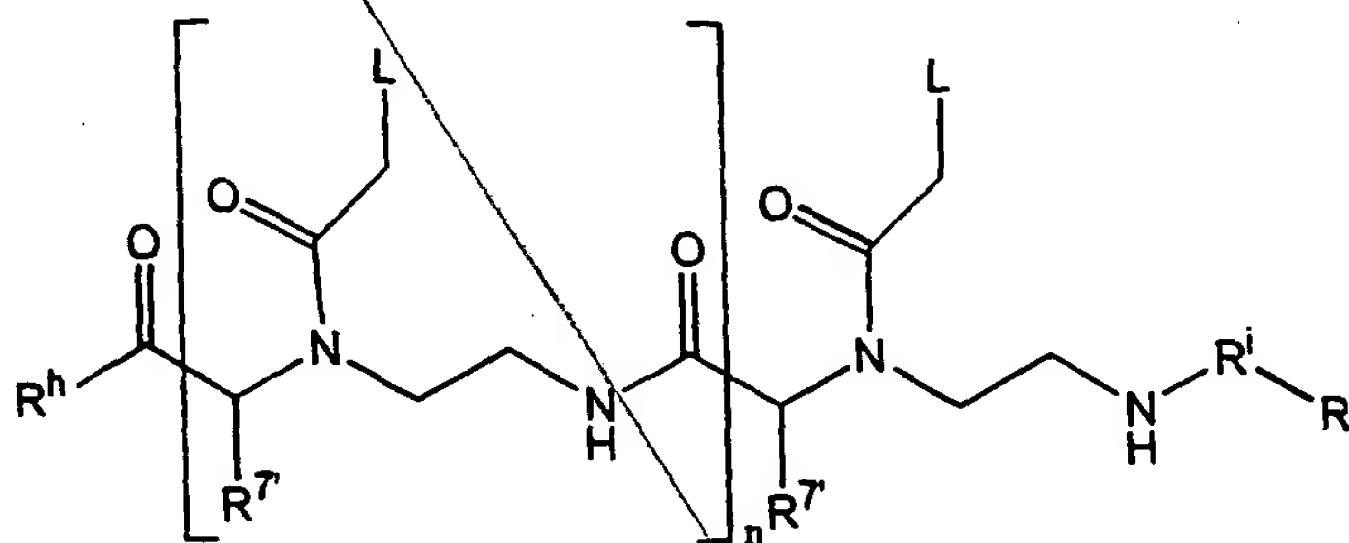
35. The method of claim 32 wherein  $R^i$  is D-lysine labeled with a fluorescent group and  $R^j$  is an adamantoyl group.

36. The method of claim 35 wherein said fluorescent group is fluorescein.

37. The method of claim 32 wherein  $R^i$  and  $R^j$ , together, are an adamantoyl group.

38. The method of claim 32 wherein  $R^7$  is the side chain of an amino acid and the carbon atom to which the side chain is attached is stereochemically enriched.

*SUB 5*  
 39. A method of treating an animal comprising administering to the animal a therapeutically effective amount of a peptide nucleic acid of formula:



wherein:

each  $L$  is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each  $R^7$  is hydrogen or the side chain of a naturally-occurring or non-naturally-



occurring amino acid, at least one  $R^7$  being the side chain of a naturally-occurring or non-naturally-occurring amino acid;

$R^h$  is OH,  $NH_2$ , or  $NHLysNH_2$ ;

each of  $R^i$  and  $R^j$  is, independently, a lipophilic group or an amino acid labeled with a fluorescent group; or  $R^i$  and  $R^j$ , together, are a lipophilic group; and

$n$  is an integer from 1 to 30.

40. The method of claim 39 wherein at least one of said  $R^7$  is the side chain of a naturally-occurring amino acid.

41. The method of claim 40 wherein at least one  $R^7$  is the side chain of D-lysine.

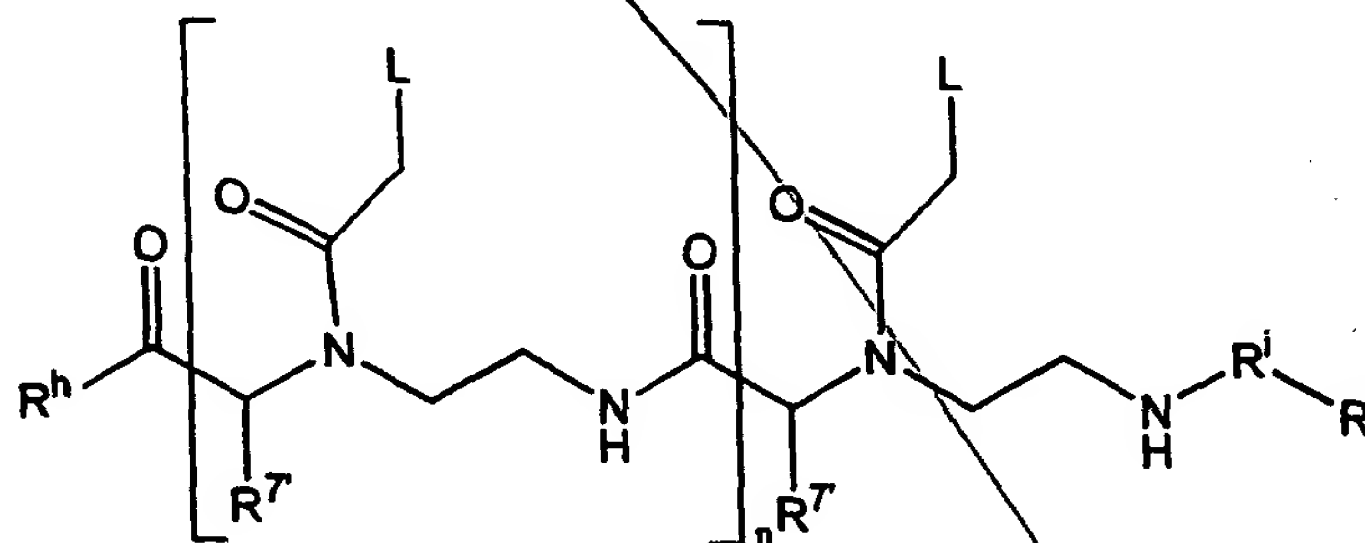
42. The method of claim 39 wherein  $R^i$  is D-lysine labeled with a fluorescent group and  $R^j$  is an adamantoyl group.

43. The method of claim 42 wherein said fluorescent group is fluorescein.

44. The method of claim 39 wherein  $R^i$  and  $R^j$ , together, are an adamantoyl group.

45. The method of claim 39 wherein  $R^7$  is the side chain of an amino acid and the carbon atom to which the side chain is attached is stereochemically enriched.

46. A method of treating an animal comprising administering to the animal a therapeutically effective amount of a composition comprising a peptide nucleic acid incorporated into a liposome, said peptide nucleic acid having formula:



wherein:

each L is, independently, a naturally-occurring nucleobase or a non-naturally-occurring nucleobase;

each R<sup>7</sup> is hydrogen or the side chain of a naturally-occurring or non-naturally-occurring amino acid;

R<sup>h</sup> is OH, NH<sub>2</sub>, or NHLysNH<sub>2</sub>;

each of R<sup>i</sup> and R<sup>j</sup> is, independently, a lipophilic group or an amino acid labeled with a fluorescent group; or R<sup>i</sup> and R<sup>j</sup>, together, are a lipophilic group; and

n is an integer from 1 to 30.

47. The method of claim 46 wherein at least one of said R<sup>7</sup> is the side chain of a naturally-occurring amino acid.

48. The method of claim 47 wherein said amino acid is D-lysine.

49. The method of claim 46 wherein R<sup>i</sup> is D-lysine labeled with a fluorescent group and R<sup>j</sup> is an adamantoyl group.

50. The method of claim 46 wherein said fluorescent group is fluorescein.

51. The method of claim 46 wherein R<sup>i</sup> and R<sup>j</sup>, together, are an adamantoyl group.

52. The method of claim 46 wherein R<sup>7</sup> is the side chain of an amino acid and the carbon atom to which the side chain is attached is stereochemically enriched.

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